Methods: Daily oral administration of letrozol (1 mg/kg body weight) for 21 consecutive days induced ovarian cysts in female rats. Effective dose of IMOD (30 mg/kg/day) was administrated intraperitoneally for 21 days. Biomarkers of ovarian function, serum estradiol (E), progesterone (P), testosterone (T) and the ovarian immunomodulator prostaglandin E (PGE) were analyzed. To determine the role of oxidative stress in PCO, the level of cellular lipid peroxidation (LPO), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), peroxynitrite (ONOO) and tumor necrosis factor alpha (TNF-α) as a marker of inflammation and apoptosis were measured in the serum and ovaries.
Results: Compared to control group, letrozole-treated group showed irregular cycles, polycystic ovaries characterized by high incidence of sub-capsular ovarian cyst with diminished or scant granulosa cell layer, luteinized granulosa cells in the cyst wall, theca cell hyperplasia, increased number of atretic pre-antral and antral follicles and absence of corpus luteum (CL). Letrozole-induced PCO in rats exhibited a significant increase in LPO and ONOO in serum and ovary while significantly decreased serum and ovarian SOD, CAT, and GPx. Also, serum T and TNF-α levels, and ovarian PGE were increased in animals with cysts compared with healthy controls, while E and P diminished. All measured parameters were improved by IMOD and reached close to normal levels.
Conclusion: The present study shows mechanistic links of oxidative stress and TNF-α in the pathogenesis of cystic ovaries indicating that development of cysts involves changes in serum and ovarian oxidant–antioxidant balance. Also IMOD is able, directly or indirectly, cope the histopathological, endocrine and biochemical alterations produced by letrozole in PCO rats. It is strongly recommended to examine selenium based agents like IMOD in the clinic concurrent with standard therapeutics to ascertain its benefit in patients undertaking PCO therapy.

Keywords: Polycystic Ovary**,** Oxidant-Antioxidant Balance

163 The Protective Effect of NAC against "Malathion – Induced" ROS Formation and Mitochondrial Dysfunction in Freshly Isolated Rat Hepatocytes

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Objective: Induction of oxidative stress by Organophosphate compounds (OPs) has been previously reported, but whether the precise mechanism of protective effects of N-acetylcysteine as a Glutathion (GSH) prodrug against Malathion–induced cell toxicity is exclusively related to its Reactive Oxygene Species (ROS) scavenging effect or not, has been investigated in the current study.
Methods: Freshly isolated rat hepatocytes were used to determine the effect of NAC on Malathion cytotoxicity. Rat hepatocytes were isolated using collagenase perfusion and cell viability, mitochondrial membrane potential (MMP) and ROS formation were determined using trypan blue exclusion, Rhodamine 123 fluorescense and fluorogenic probe, 2', 7' - dichlorofluorescin diacetate (DCFH-DA), respectively.
Results: Despite the protective effect of NAC on cell viability and MMP in both groups treated with Malathion 1 and/or 1.5 mM, its efficacy against ROS formation was only seen in the first one. The occurrence of mitochondrial dysfunction besides the oxidative stress in Malathion-induced cytotoxicity was confirmed.
Conclusion: Other mechanisms in addition to ROS scavenging for beneficial effects of NAC against OPs toxicity is proposed.